REMARKS

Claims 1-26 are currently before the examiner. Claims 13-15 and 24-26 have been withdrawn by the examiner as, in the examiner's view, being drawn to separate and distinct invention. Applicant traversed the withdrawal, which the examiner did not deem persuasive. Claims 1-12 and 16-23 stand rejected.

Double patenting

The examiner has maintained the non-statutory double patenting rejection of claims 16-23 over claims 1-7 of U.S. Pat. No. 5,762,957. The examiner states that the inventions are not patently distinct for reasons of record as set forth in the 29 November 2007 office action.

The examiner augments the previous grounds for the double patenting rejection by stating that applicant's remarks are non-persuasive regarding the differences between the current kits and those of the '957 patent. In the examiner's view, the current kit and the '957 kit "are claiming the same components in both kits" and therefore would produce the same results.

Applicant traverses.

Applicant's response

Applicant maintains and incorporates herein the rationale presented in the response to the 29 November 2007 office action for finding the kits of the current application and those of the '957 patent patently distinct are valid. That is,

> The kit of the current claims require a first compartment containing an acidic or basic buffer solution both within and outside lipid-like vesicles, wherein the vesicles are substantially impermeable to the buffer for at least one-quarter hour following loading of the chemical species and, further, the first solution has a pH selected such that the stability of the vesicle and its buffer can be maintained for a period of at least one week at 4 °C. The current claims also require a second compartment having a second solution at a selected pH wherein when the first and second solutions are mixed the resulting solution has a pH that is 0.5, 0.3 or 0.2 pH units above the pH of the buffer in the liposomes if the buffer is acidic or 0.5, 0.3 or 0.2 pH units below the pH of the buffer in the liposomes if the buffer is basic.

> The patented kits, on the other hand, make no mention whatsoever as to the duration of the impermeability of its liposome membranes to the buffer or to the selection of a first solution pH so as to result in stable vesicles and buffers for at least one week. Further, the patented invention says nothing about the pH of the combined first and second solutions. Thus the patented kit requires only acids and bases and does not specify any particular pH while the current application does. The difference, i.e., from no preference to the express limitations of the current invention are not obvious.

Applicant emphasizes that the components of the kits are not the same. The current kits require a very specific relationship between the pHs of the first and second solutions which is nowhere evident in the kit components of the '957 patent.

Further, the kits of the current invention require that the pH of the first solution be such that "the stability of the vesicle and its buffer can be maintained for a period of at least one week at 4 °C, which element is completely absent from the kits of the '957 patent. The mere fact that the possibility of such a composition is disclosed in the '957 patent specification is of no import. The '957 kit claims do not claim such. To suggest that the kits of the '958 patent would "produce the same results" without virtually any of the specific limitations of the current kits would be to incorporate limitations from the specification into the claims, which the examiner is well aware is impermissible.

The examiner is requested to reconsider and thereupon withdraw the terminal disclaimer over U.S. Pat. No. 5,762,957.

35 U.S.C. §112, first paragraph rejection of claims 1-8, 10-12 and 16-23

The examiner has rejected claims 1-8, 10-12 and 16-23 under §112, first paragraph, because, in the examiner's view, the specification "fails to provide sufficient written bases of any of the agents demonstrating wherein possession of use of the broad terms: a chemical species, an amino group, an amine, a drug, a first substance, and a second substance."

Applicant traverses.

Applicant's response

Applicant is not laying claim to certain chemical species, amines, drugs and the like. Rather, applicant is claiming a general purpose method of loading acid and basic

chemical species into lipid-like vesicles. Contrary to the examiner's position, there is no authority stating that a single example is insufficient to support a general method claim absent compelling reasons to lead one of ordinary skill in the art to believe that the method would not work with most if not all other species of the exemplified substance. Specifically, the term "chemical species" is not used in the claim anywhere without ultimately being modified for the purpose or the claim as being an acidic or basic chemical species or a chemical species containing an "acid pH responsive" or a "basic pH responsive" group. This is a sufficient description to permit those skilled in the art to immediately envision the types of acidic/basic chemical species or acid/basic pH responsive groups since pH is a fundamental concept of organic chemistry known to all practitioners of the organic chemical art. The chemical species are further defined in the specification at page 3, paragraph [0023] and page 4, paragraph [0030]:

> [0023] ... The term chemical species having one or more selected acid or basic pH responsive groups is also used broadly to indicate any chemical or drug having acid or basic groups, properties or functions such as, but not limited to amine or carboxyl groups. Other substances such as imidazoles and barbituric acid derivatives may also be used. The term also includes any chemical that has desired chemical or therapeutic properties that will not be sufficiently altered by attachment of such pH responsive groups. ...
>
> [0030] ... The chemical [species] loading rate will depend on the pKa and will be complete within less tha minute for low molecular weigh (MW less than 500) amine chemicals with pKs's less than 10 and having no charge or strongly polar groups other than the amino group. Analogously, weak acids [chemical species] having pKas greater than 4 will accumulate in the liposomes in about one minute, unless they bear strong polar groups other than their carboxyls.

Applicant believes that no more is required to sufficiently explicate what is meant by "chemical species."

"Amino" and "amine" need no further definition. Those skilled in the art will immediately understand these terms to refer to a –NRR' group wherein R and R' are independently hydrogen, alkyl and/or aryl and to compounds containing such group and would likewise immediately know that the group or compound will have a basic pH.

Such commonly-known terms do not require definition in an application unless the usage there is different from what those skilled in the art would expect. Such is not the case here. Example 1 provides a specific basic entity, Tempamine, which would be immediately recognized by those skilled in the art to be an "amine" and to contain one or more "amino" groups, to demonstrate the fundamental operation of the claimed method. There is nothing to suggest that other amines would not work.

With regard to drugs, more than sufficient examples are provided. In paragraph [0023], it is stated:

> [0023] ... The terms chemical species and "drugs" include but are not limited to, such substances as chemicals, drugs for chemotherapy and immunosuppression, membrane permeable peptide toxins and hormones. Examples of drugs having molecules having basic properties are vincristine, doxorubicin, streptomycin, chloroquine and daunorubicin. Examples of drugs having molecules having acid properties are derivatives of methotrexate, daunomycin, penicillin, p-amino salicylic acid and salicylic acid derivates.

Methotrexate is exemplified in Example 4. Applicant maintains that no more description is necessary or warranted. The method is intended to be broadly applicable to any chemical species having the requisite properties and there is nothing to suggest that its applicability is any less expansive than claimed and described.

35 U.S.C. § 103 rejection of claims 1-12

The examiner has rejected claim 1-12 as being unpatentable over Nichols, etal, or Deamer, et al, or Cramer, et al. The examiner states that each of these references teaches the concept of loading a chemical species into the liposomes using a pH gradient and that it would have been obvious to one skilled in the art to load any drug with the expectation of similar loading since applicant has not demonstrated side-by-side comparison of the prior art's liposome loading versus the present application's liposome loading.

Applicant traverses.

Applicant's response

As applicant pointed out in his response to the 19 November 2007 office action to the §102 rejections over Nichols, Deamer and Cramer, applicant does not dispute that

using pH gradients to load vesicles. Applicant pointed out, and reiterates here, that nowhere in Nichols, Deamer or Cramer is the concept taught or so much as suggested of using membrane impermeable buffers to maintain loading after the gradient is destroyed. Since none of the cited references individually teaches or suggests such, clearly the combination of them cannot do so.

The examiner is requested to reconsider and thereupon withdraw the rejection.

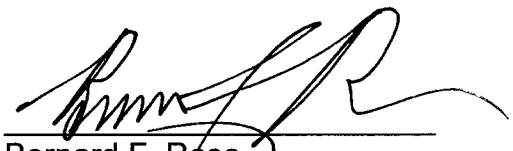
CONCLUSION

Applicant believes that based on the above Remarks, this application is in condition for allowance and respectfully requests that it be passed to issue.

In addition, applicant requests a one month extension in time within which to file this response. The Commissioner is authorized to charge the fee due to SQUIRE, SANDERS & DEMPSEY Deposit Account No. 07-1850.

Dated: January 5, 2009

Respectfully submitted,



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